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EFFECTS OF A β-ANDRENERGIC AGONIST ON GROWTH PERFORMANCE, BODY COMPOSITION AND NUTRIENT RETENTION IN FINISHING PIGS FED NORMAL OR LOW AMOUNTS OF PROTEIN

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ABSTRACT

In earlier studies with pigs the β-adrenergic agonist Ro 16-8714 (β-AG) enhanced the efficiency of nitrogen (N) retention. Therefore effects of Ro 16-8714 were studied on growth rate, body composition, N, fat and energy retention in pigs fed isoenergetically, but given different amounts of protein (112 or 138 g/kg diet) without (groups LP and NP) or with 60 mg Ro 16-8714 per kg diet (groups LPβ and NPβ) from 60 to 100 kg live weight. Weight gain (898, 927, 855 and 810 g/day in NP, NPβ, LP and LPβ) decreased, whereas food : gain ratio (2·94, 2·82, 3·04 and 3·24 kg/kg in NP, NPβ, LP and LPβ) was increased by low protein intake ($P < 0·05$) and both weight gain and food conversion were modified by the interaction (P × β) of protein intake and Ro 16-8714 ($P < 0·05$). Killing-out proportion (820, 830, 830 and 830 g/kg in groups NP, NPβ, LP and LPβ) was modified by protein intake and Ro 16-8714 ($P < 0·05$). Carcass growth rate (760, 814, 748 and 723 g/day in NP, NPβ, LP and LPβ) was modified by protein intake and by P × β ($P < 0·05$), while non-carcass growth rate (90, 77, 76 and 56 g/day in NP, NPβ, LP and LPβ) was changed by protein intake and by Ro 16-8714 ($P < 0·05$). Compared with NP, weights of kidneys (−0·025 kg), small intestine (−0·26 kg) and large intestine (−0·17 kg) were decreased by low protein feeding, and weights of heart, spleen and stomach decreased in response to Ro 16-8714 (−0·02, −0·02 and −0·06 kg; $P < 0·05$) while both low protein intake and Ro 16-8714 reduced liver weight (−0·12 and −0·23 kg, respectively; $P < 0·05$) and blood volume obtained at slaughter (−0·12 and −0·23 kg; $P < 0·05$). Carcass N (1813, 1970, 1786 and 1825 g in NP NPβ, LP and LPβ) increased in response to Ro 16-8714, but was reduced by low protein intake ($P < 0·05$), while non-carcass N (330, 309, 312 and 285 g in NP, NPβ, LP and LPβ) was decreased by both low protein intake and Ro 16-8714 ($P < 0·01$). Carcass and non-carcass fat (22·1, 19·9, 23·4 and 23·0 kg, respectively 1·51, 1·41, 1·59 and 1·68 kg in NP, NPβ, LP and LPβ) increased with low protein feeding ($P < 0·05$), but were not significantly influenced by Ro 16-8714. The efficiency of N retention (295, 363, 321 and 327 g/kg N retained : N intake in NP, NPβ, LP and LPβ) was enhanced by Ro 16-8714 ($P > 0·05$) whereas the efficiency of energy retention was not influenced by Ro 16-8714 and protein intake. In conclusion, an adequate intake of protein is necessary for optimum expression of many, but not all, effects of the β-adrenergic agonist Ro 16-8714.

KEYWORDS: β-adrenergic agonists, body composition, growth, protein intake, pigs.

INTRODUCTION

SEVERAL β-adrenergic agonists (β-AG) have been termed repartitioning agents for their ability to reduce fat retention while enhancing protein accretion in various species, including pigs (Ricks, Dalrymple, Baker and Ingle, 1984; Hanrahan, Quirke, Bomann, Allen, McEwan, Fitzsimons, Kotzian and Roche, 1986; Fiems 1987; Williams, 1987 and 1988; Berschauer, Klotz and Greife, 1987; Berschauer, 1989). The effects on body composition are of potential interest in meat animal production, especially during the finishing period, and in humans for treatment of obesity, diabetes mellitus and possibly even muscle wasting disease.

Mechanisms by which β-AG may change body composition and modify growth performance are still not fully understood, as reviewed by Fiems (1987), Williams (1987 and

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1988) and Berschauer (1989). The effects on fat tissue are variable and have been reported to involve enhanced lipolysis and/or reduced lipogenesis and in part increased triglyceride turn-over rate. In some, but not all, studies reduction of fat cell number and/or fat cell size has been reported as well as changes in tissue fatty acid composition (relative increase of unsaturated fatty acid concentration). Enhanced muscle growth is thought to be due to increased protein synthesis or reduced protein degradation or both and has been associated with changes in skeletal muscle fibre composition (relative or absolute increase of type II fibres). β-AG mediate their effects on various organs, including muscle and fat tissue, directly through β-adrenergic receptors and indirectly by modifying the activity of endocrine systems such as insulin (Buttery and Dawson, 1987; Blum and Flückiger, 1988; Orcutt, Cline and Mills, 1989). Metabolic, endocrine, cardiovascular, respiratory and skeletal muscle activities are initially markedly altered, but such changes rapidly disappear during continued exposure to β-AG due to development of tachyphylaxis (Blum and Flückiger, 1988; Mills and Orcutt, 1989; Zimmerli and Blum, 1990). This indicates that chronic metabolic effects, leading to changes in body composition and growth performance, are largely due to intracellular changes. Chronic effects of repartitioning agents may be mediated by receptors other than β_2- or β_1-subtypes. The effects of β-AG are variable and depend on the structure of the β-AG, duration of application, anatomical location, age, species, breed, sex and also nutritional factors.

The β-AG Ro 16-8714 was shown to have acute thermogenic, lipolytic, glycogenolytic and insulinogenic effects and to increase heart rate in man (Henny, Schutz, Buckert, Meylan, Jéquier and Felber, 1987), as reported for other β-AG. During prolonged application Ro 16-8714 reduced fat content, slightly enhanced nitrogen (N) retention and had anti-diabetogenic activity in rats (Meier, Alig, Buergi-Saville and Mueller, 1984). Furthermore, Ro 16-8714 enhanced the efficiency of N utilization in a dose-dependent manner under restricted and *ad libitum* feeding conditions in finishing pigs (Bracher-Jakob, Stoll and Blum, 1990).

The N-sparing of β-AG offers the possibility of normal growth performance despite feeding reduced amounts of protein, on the assumption that the efficiency of N utilization would not be reduced. In finishing pigs receiving Ro 16-8714 the protein content of the diet could have theoretically been decreased from 140 to 113 g/kg (i.e. by 1/5) without reducing growth performance (Bracher-Jakob *et al.*, 1990). Based on that premise, the present study was designed to investigate the effects of Ro 16-8714 on performance, body composition and nutrient retention in pigs given low or adequate amounts of protein.

MATERIAL AND METHODS

Experimental design and feeding

Forty castrated Large White pigs were individually housed at the Swiss Federal Research Station for Animal Production, Grangeneuve. Pigs were balanced across treatments for initial body weights and age. They were used in a 2 × 2 factorial experiment with eight complete weight blocks. An additional eight pigs constituted the reference group and were slaughtered at 60 kg body weight (BW). After the pre-fattening period, at 60 kg BW, pigs were allocated to four treatment groups given diets containing 138 or 112 g crude protein per kg without (groups NP and LP, respectively) or

TABLE 1

Chemical composition and nutrient concentrations of finishing diets

	Experimental groups			
	NP	NPβ	LP	LPβ
Dry matter (g/kg)†	879·0	883·0	880·0	882·0
Gross energy (MJ/kg)	16·2	16·2	16·2	16·2
Digestible energy (MJ/kg)	13·5	13·4	13·5	13·4
Protein (g/kg)	139·8	135·9	113·5	110·6
Lysine (g/kg)	7·7	8·1	6·2	7·4
Methionine + cystine (g/kg)	5·3	5·6	4·9	4·3
Calcium (g/kg)	6·0	n.d.	5·9	n.d.
Phosphorus (g/kg)	4·4	n.d.	4·1	n.d.

† Dry matter expressed on a fresh-weight basis; all other measurements expressed on air-dry basis.

with the β-AG (groups NPβ and LPβ, respectively). Although Ro 16-8714 was added to a pre-mix in amounts to attain 60 mg/kg in the finishing diet, only 50 mg/kg diet were detectable by assay.

The finishing diets (offered from 55 to 100 kg BW) contained wheat, maize, barley, soya-bean meal, fat, minerals, salt, vitamin pre-mix, lysine, methionine; the chemical composition of the four finishing diets is shown in Table 1. Dextrose (30 g/kg) was added to overcome the bitter taste of the β-AG. Pre-fattening and finishing diets did not contain antimicrobial agents. It was not possible to pellet the finishing diets due to heat sensitivity of the β-AG.

Pigs were allowed to adapt to the finishing control diet (140 g crude protein per kg) for 1 week before they were assigned to treatments at 60 kg BW. They were given food twice daily. Restricted feeding guaranteed an identical food intake. Daily food allowances were adjusted weekly and increased from 1·03 kg/day at 25 kg BW to 2·4 kg/day at 61 kg BW and to 2·8 kg/day from 86 kg BW until slaughter. Pigs were weighed once weekly in the morning prior to feeding.

Slaughter procedure

After an overnight fast, the animals weighing about 100 kg BW were brought to the slaughterhouse of the research station. Pigs were stunned by electroshock, weighed and exsanguinated. They were re-weighed to obtain data on blood losses to estimate blood volume. A blood sample of 0·5 l was frozen until chemically analysed. The snout was tied to prevent aspiration of scalding water. The intact alimentary tract and bladder were removed, weighed, emptied of all contents, extensively rinsed with tap water, allowed to drain and re-weighed. The weight loss represented the gut fill. In addition, stomach, small and large intestine, and spleen were weighed. The intestinal fraction comprised stomach, small and large intestine, bladder, genitals and mesentery. Organs were removed and weights of heart (blood residues removed), lungs, liver (gall bladder emptied), and kidneys were recorded. The organ fraction included the above organs plus spleen, eyes and auditory canals removed from the head, oesophagus, spinal cord, heart, blood and bile. Intestinal and organ fractions were ground separately with a mincer and samples of 400 g were deep-frozen at −18°C until further processing.

The carcass was split along the spinal cord and each half was weighed to give the hot carcass weight. Killing out, defined as the ratio of hot carcass weight (including head and kidneys) to body weight, was recorded. The carcass was cooled at 2°C for 4 h. Before dissection, the halves of the carcass were re-weighed to estimate water loss. Backfat thickness was measured at three locations on the right half: (1) on the thickest point over the shoulder; (2) on the thinnest point of the back; (3) three times over the *m. gluteus medius,* the average backfat thickness being the mean of (1), (2) and (3). The right half of the carcass was dissected to give subcutaneous (trimmed) fat of ham, shoulder and loin, premium cuts (ham, shoulder, loin), belly, kidney and pelvic fat, neck, head and feet. The corresponding weights were recorded. The left carcass half (including the internal fat) and the head were deep-frozen for at least 1 week at −18°C and later re-weighed and sawed cross-sectionally at intervals of 3 cm for chemical analysis using sawdust residues collected quantitatively and stored at −18°C until analysed. Empty body composition represented the sum of subfractions (organs, intestine, carcass, head, blood) plus claws as well as bristles. As determined in previous studies (Bracher-Jakob *et al.,* 1990), bristles and claws of 60-kg and 100-kg pigs weighed 148 g and 226 g dry matter (DM), respectively, and contained 158 g N, 23 g crude fat, 10 g ash and 23·3 MJ gross energy (GE) per kg DM, i.e. 10 g/kg or less of N, fat and GE stored in the body.

Chemical analysis

In foods, the amounts of DM was obtained by weight loss analysis, N was measured by the Kjeldahl procedure and (crude) fat was determined after extraction with petroleum benzene at a boiling range of 40 to 60°C. The GE content was analysed using an adiabatic bomb calorimeter. Amino acids

were measured using chromatographic separation by a Beckman, model 119 CL amino acid analyser. Calcium was determined by atomic absorption spectrophotometry and inorganic phosphorus was measured by a calorimetric method. Updated methods used for the determination of food components are described in detail in the 'Methodenbuch der eidgenössischen landwirtschaftlichen Forschungsanstalten' (unpublished).

Frozen samples of all body fractions were freeze-dried to measure DM content and later homogenized. The DM concentration of carcass and head was subsequently adjusted for evaporative water losses occurring during cooling and freezing. Cooling loss averaged 11·5 g/kg hot carcass and freezing loss equalled 8·5 g/kg cold carcass and 10·4 g/kg cold head. Ash, N, fat and GE were measured using the same procedures as for foods. In addition, non-protein nitrogen (NPN) was analysed in all body fractions by heating 2 g samples in distilled water for 5 min, precipitation of proteins by the addition of copper sulphate and sodium hydroxyde and N determination of the filtrate as described above. Pure protein content was the difference between total N and NPN

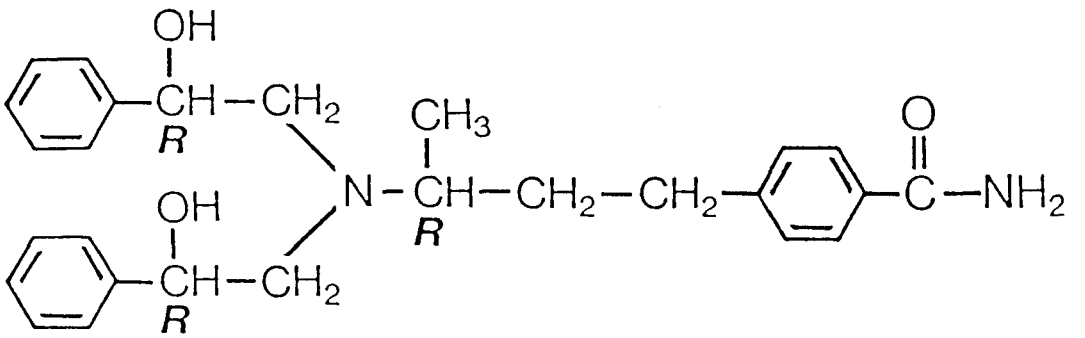

FIG. 1. Structure of the β-adrenergic agonist Ro 16-8714 (molecular weight = 432·56).

TABLE 2

Effects of Ro 16-8714 on growth, food intake and food utilization of finishing pigs given normal or low amounts of protein

	Experimental groups								
	NP		NPβ		LP		LPβ		
	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Significance†
Total food intake‡ (kg)	117·2	14·4	115·8	16·9	124·8	9·3	127·2	14·9	P*
Weight gain (g/day)	889·4	60·7	927·1	69·5	855·1	27·6	810·0	69·5	P**, P × β*
Food : gain (kg/kg)	2·94	0·19	2·82	0·23	3·04	0·10	3·24	0·23	P**, P × β*
Killing out§ (g/kg)	820·5	6·6	830·2	6·6	829·0	8·7	835·0	8·3	P*, β**
Dissectable fat‖ (g/kg)	171·3	16·9	154·2	18·2	176·9	10·3	161·8	10·0	β**
Carcass : empty body (g/kg)	783·1	5·5	792·8	3·8	794·1	9·1	799·3	6·4	P**, β**
Non-carcass : empty body (g/kg)	141·7	5·2	133·4	3·4	135·8	4·9	128·6	7·7	P*, β***
Carcass growth rate (g/day)	760·1	47·1	814·0	57·2	748·3	26·0	723·4	57·7	P**, P × β*
Non-carcass growth rate (g/day)	90·38	13·60	77·41	8·96	76·53	11·11	56·21	16·08	P***, β***

† In this and subsequent tables significance of effects: P, protein effect; β, effect of Ro 16-8714; P × β, interaction between protein and Ro 16-8714.
‡ From 60 to 100 kg.
§ Hot carcass.
‖ Trimmed (subcutaneous, kidney and pelvic) fat.

concentrations and NPN : N ratios were calculated as an indication of pure protein content of the different tissues.

β-adrenergic agonist

The β-adrenergic agonist P-[(R)-3-[bis-[(R)-β-hydroxyphenetyl] amino]butyl]benzamide (Ro 16-8714) was a gift from F. Hoffmann-la Roche AG, Basle. Its structure is shown in Figure 1 and with three atomic rings is different from that of other β-AG used so far as repartitioning agents in farm animals.

Statistical analysis

Data were analysed by two-way analysis of variance (WIDAS program, Dr Wälti AG, Buchs, Switzerland, revised 1986). One pig of group NP was withdrawn from the experiment because of severe leg weakness and degrees of freedom were adjusted accordingly. Results are expressed as means with standard deviations.

RESULTS

Growth performance, food conversion and carcass dissection

Initial and final weights of the four experimental groups (60·8 and 101·1 kg, respectively) were similar. The total food intake during the entire experimental period of groups given low amounts of protein was higher than in pigs given adequate amounts of protein ($P < 0·05$) because more time (+4 days) was required to reach the slaughter weight. The average daily intake was identical in all groups (2·66 kg/day). Daily gain of pigs receiving the low protein diet was reduced compared with those given adequate amounts of protein ($P < 0·01$). The addition of the β-AG enhanced daily gain of animals given adequate amounts of protein, whereas weight gain of the group given low amounts of protein was reduced, resulting in a negative interaction between protein intake and β-AG ($P < 0·05$).

Low protein feeding resulted in an increased food : gain ratio compared with the group receiving the adequate protein diet ($P < 0·01$). In the presence of the β-AG, food : gain ratio was depressed in the group given adequate amounts of protein, but elevated in the low protein group, leading to an interaction between protein in the diet and β-AG ($P < 0·05$).

Gut fill (mean 34·3 g/kg BW and 1240 g/kg daily food intake prior to slaughter) did not differ between groups and thus did not mask treatment effects. Killing-out proportion and carcass : empty body ratio were both increased by low protein diet ($P < 0·05$) and β-AG ($P < 0·01$). The head fraction of empty body was distinctly reduced by low protein feeding ($P < 0·001$; not shown). The non-carcass : empty body ratio was reduced by both protein intake and β-AG.

The portion of valuable meat cuts (ham, shoulder and loin) in the cold carcass was increased by the β-AG independent of protein supply (NP, 517 (s.d. 17) g/kg; NPβ, 544 (s.d. 17) g/kg; LP, 515 (s.d. 18) g/kg; LPβ, 530 (s.d. 21) g/kg; $P < 0·05$) and the portion of dissectable fat was correspondingly reduced by the β-AG ($P < 0·05$). The internal fat portion (kidney and pelvic fat) increased when low amounts of protein were given ($P < 0·001$), but decreased in the presence of the β-AG ($P < 0·05$), whereas average backfat thickness (28 mm) remained unaffected by treatments.

Carcass growth rate was increased in the presence of the β-AG in pigs given adequate amounts of protein, but decreased in pigs given the low protein diet, leading to a negative interaction between β-AG and dietary protein ($P < 0·05$). Low protein intake plus β-AG decreased non-carcass growth rates in an additive manner ($P < 0·001$).

Weight of organs and intestine

As shown in Table 3, all organs, except the lungs, responded negatively to low protein intake and/or to the β-AG ($P < 0·05$). Both treatment factors caused reduced weights of liver and blood obtained at slaughter in an additive manner ($P < 0·05$). Heart, spleen and stomach were only influenced by the β-AG ($P < 0·05$), while kidneys, small and large intestine weights only reacted to low protein supply ($P < 0·05$), the small intestine being especially susceptible to low protein supply ($P < 0·001$).

TABLE 3

Effects of Ro 16-8714 on organ weights of finishing pigs given normal or low amounts of protein

	Experimental groups								
	NP		NPβ		LP		LPβ		
	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Significance†
Lungs (kg)	1·013	0·125	1·003	0·235	1·131	0·194	1·047	0·117	
Heart (kg)	0·334	0·034	0·318	0·024	0·358	0·026	0·314	0·017	β**
Liver (kg)	1·710	0·136	1·591	0·143	1·584	0·154	1·481	0·114	P**, β**
Kidneys (kg)	0·273	0·028	0·267	0·027	0·253	0·018	0·248	0·016	P**
Spleen (kg)	0·145	0·031	0·126	0·019	0·139	0·020	0·119	0·026	β*
Blood volume (kg)	3·47	0·48	3·23	0·27	3·27	0·27	2·87	0·47	β*
Stomach (kg)	0·56	0·11	0·50	0·04	0·54	0·08	0·50	0·05	β**
Small intestine (kg)	1·57	0·22	1·56	0·19	1·39	0·08	1·31	0·09	P***
Large intestine (kg)	1·43	0·18	1·36	0·15	1·33	0·20	1·26	0·12	P*

† See Table 2.

TABLE 4

Effects of Ro 16-8714 on partitioning of chemical components in the carcass and non-carcass fractions of finishing pigs given normal or low amounts of protein

	Experimental groups								
	NP		NPβ		LP		LPβ		
	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Significance†
Carcass nitrogen (N)† (g)	1813	86	1970	125	1786	84	1825	80	P*, β**
Carcass fat† (g)	22080	2696	19948	2622	23425	2409	22966	1094	P*
Non-carcass N (g)	330	21	309	9	312	13	285	18	P**, β**
Non-carcass fat (g)	1515	317	1410	148	1594	252	1680	0·260	P*
Carcass N: total N† (g/kg)	832	5	851	9	837	10	850	8	β***
Carcass fat: total fat† (g/kg)	936	8	933	6	936	4	932	8	

† See Table 2.
‡ Head included.

Chemical composition of body fractions, partitioning of chemical components and nutrient retention

N content in groups NP, NPβ, LP and LPβ of organs (101 (s.d. 5), 102 (s.d. 4), 99 (s.d. 6) and 97 (s.d. 4) g/kg, respectively), intestine (51 (s.d. 9), 50 (s.d. 4), 46 (s.d. 5) and 42 (s.d. 4) g/kg, respectively) and carcass (51 (s.d. 5), 58 (s.d. 6), 49 (s.d. 4) and 50 (s.d. 2) g/kg, respectively) was decreased by low protein intake ($P < 0·05$), but increased by Ro 16-8714 in the carcass fraction ($P < 0·05$). N content of blood (mean 161 g/kg) was not changed.

The NPN : N ratio of organs, intestine and carcass (mean 60, 387 and 98 g/kg, respectively) was not changed by protein intake or by Ro 16-8714, but NPN : N ratio of blood (12·1 (s.d. 1·4), 12·9 (s.d. 1·3), 12·3 (s.d. 1·6) and 10·5 (s.d. 2·2) g/kg in groups NP, NPβ, LP and LPβ, respectively) was influenced by protein intake ($P > 0·05$) and by the interaction of protein intake and β-AG ($P < 0·05$).

Fat content in groups NP, NPβ, LP and LPβ of organs (237 (s.d. 40), 221 (s.d. 19), 244 (s.d. 38) and 266 (s.d. 29) g/kg, respectively), intestine (652 (s.d. 57), 658

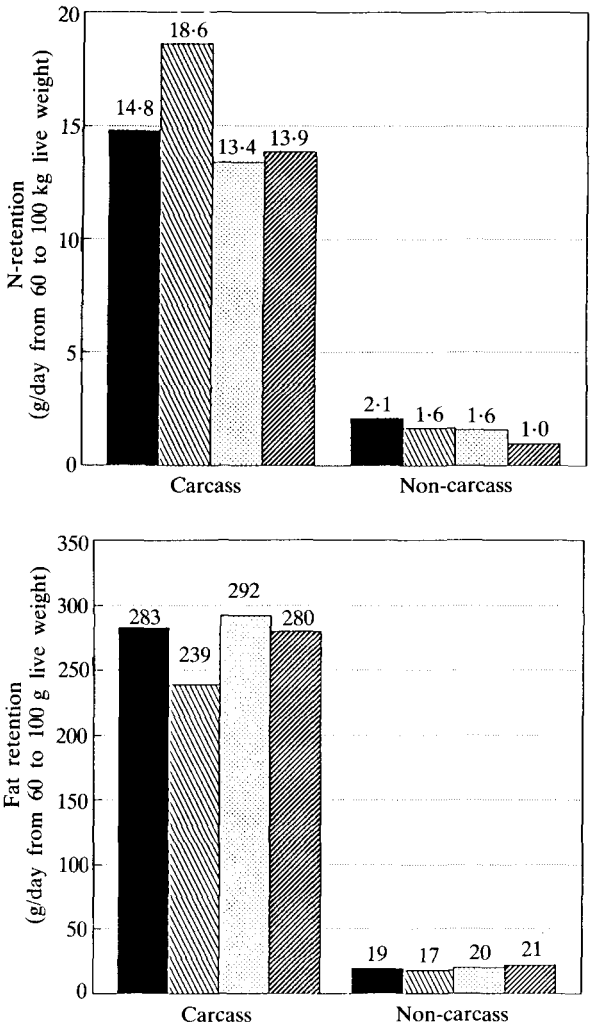

FIG. 2. Nitrogen and fat retention in the carcass and the non-carcass fraction of pigs during the finishing period from 60 to 100 kg in pigs given normal or low amounts of crude protein (138 g or 112 g crude protein per kg diet) without (groups NP ■ and LP □, respectively) or with the β-adrenergic agonist Ro 16-8714 (groups NPβ ▨ and LP ▨, respectively).

(s.d. 35), 687 (s.d. 39) and 714 (s.d. 31) g/kg, respectively), carcass (618 (s.d. 40), 578 (s.d. 38), 636 (s.d. 31) and 630 (s.d. 16) g/kg, respectively) and blood (5·8 (s.d. 0·7), 6·3 (s.d. 0·9), 6·3 (s.d. 0·9) and 6·7 (s.d. 0·8) g/kg) was increased by low protein feeding ($P < 0·05$ for organs, intestine and carcass; $P > 0·05$ for blood) and decreased in the presence of Ro 16-8714 in the carcass ($P > 0·05$).

As shown in Table 4, carcass and non-carcass fractions of pigs given the low protein diet contained less N and more fat than adequately fed pigs ($P < 0·05$). The β-AG increased total N in the carcass, dependent on protein intake (interaction, $P > 0·05$), while N in the non-carcass fraction was reduced by both β-AG and by low protein feeding ($P < 0·01$). More N of total N was deposited in the carcass of pigs receiving the β-AG compared with control pigs ($P < 0·001$), while the carcass fat : total fat ratio only tended to decrease ($P > 0·05$).

As shown on Figure 2, daily N-retention (from 60 to 100 kg) in the carcass of β-AG treated pigs was enhanced, but considerably more was retained in those fed adequate compared with those fed low amounts of protein ($P > 0·05$). This led to a positive interaction between Ro 16-8714 and protein intake ($P < 0·01$), whereas daily N-retention in the non-carcass fraction was additively depressed ($P < 0·01$). Daily fat retention tended to be reduced by the β-AG, but not significantly and tended to have more of an effect in pigs given adequate amounts of protein, whereas daily fat retention was not changed in the non-carcass fraction.

Efficiency of energy and N conversion

Gross efficiency of N and energy conversion were calculated as the ratio of retention : intake during the finishing period (Table 5). Food N tended to be more efficiently used in the presence of the β-AG if adequate amounts of protein were given ($P > 0·05$). Efficiency of GE conversion

TABLE 5

Effects of Ro 16-8714 on gross efficiency of nitrogen (N) and gross energy (GE) conversion of finishing pigs given normal and low amounts of protein†

	Experimental groups			
	NP	NPβ	LP	LPβ
N retained: N intake (g/kg)	295 (52)	363 (60)	321 (42)	327 (32)
GE retained: GE intake (g/kg)	333 (37)	302 (45)	337 (37)	326 (32)

† s.d. in parentheses.

remained unaffected by β-AG or protein intake as were daily energy retention (not shown). Energetic efficiency and protein : fat ratio of weight gain were negatively correlated ($r = -0{\cdot}77$). Food conversion ratio was rather closely correlated with protein : fat ratio of empty body weight gain ($r = -0{\cdot}61$; $P < 0{\cdot}05$), but not with gross efficiency of energy retention.

DISCUSSION

General aspects

It is well documented and supported by the present study that in pigs restricted protein supply decreases weight gain, lean tissue growth, carcass growth and N accretion, but is associated with enhanced fat retention and increased food : gain ratio (Hennig, Wuensche, Meini, Borgmanns, Kreienbring and Bock, 1982; Wuensche, Meini, Hennig, Kreienbring and Bock, 1982; Zhang, Partridge and Mitchell, 1982; Hofstetter, 1987; Campbell, Taverner and Curic, 1988). The non-carcass weight was more reduced in the group receiving low than in the one receiving adequate amounts of protein. Davey and Bereskin (1978) also reported lower liver and kidney weights and Mersmann, Hu, Pond, Rule, Novakovsky and Smith (1987) found lower kidney weights in pigs given low protein diets. Weight reduction of the intestine, particularly of the small intestine, was impressive. The non-carcass fraction is metabolically very active (Visek, 1978; Webster, 1989) and therefore likely reacts rapidly and markedly to low protein intake, as shown in this study.

In pigs given adequate amounts of protein, Ro 16-8714 had effects which were typical for a β-AG or a repartitioning agent. It changed body composition by reducing fat retention and by enhancing N (hence protein) accretion in the carcass, carcass : empty body ratio, carcass growth rate, killing out and the amount of valuable meat cuts. In addition, while Ro 16-8714 reduced N retention in the carcass, it reduced N retention in the non-carcass fraction, i.e. altered N distribution within the N-pool, in accordance with previous studies in pigs, calves and sheep (Williams, Pagliani, Innes, Pennie, Harris and Garthwaite, 1987; Kim, Lee, Garrett and Dalrymple, 1989; Bracher-Jakob *et al.*, 1990). Whereas the efficiency of N retention was increased, the efficiency of GE utilization was not affected by the β-AG, but energetic efficiency and food : gain ratio were rather closely and negatively related to protein : fat ratio of weight gain or empty body, thus confirming previous results (Bracher-Jakob *et al.*, 1990). Ro 16-8714 also reduced the volume of blood obtained at slaughter and weights of heart, liver, spleen and stomach and therefore weight and growth rate of the non-carcass fraction. In a previous study only spleen weight and volume of blood obtained at slaughter were reduced when Ro 16-8714 was administered to pigs (Bracher-Jakob *et al.*, 1990), however there are also reports of reductions in weight of heart, liver and kidneys (Jones, Easter, McKeith, Dalrymple, Madock and Bechtel, 1985; Moser, Dalrymple, Cornelius, Pettigrew and Allen, 1986) and Mersmann *et al.* (1987) found lower stomach weight when β-AGs other than Ro 16-8714 were administered. Effects of Ro 16-8714 on growth performance and body composition were small, in accordance with previous data (Bracher-Jakob *et al.*, 1990). However, effects of β-AG other than Ro 16-8714 on growth performance have not been tested in our breed line. Because the animals were intensively genetically selected for high growth rates and low backfat thickness, large additional effects of the β-AG could not be expected.

Interactions between β-AG and protein intake

In our study the significant interactions between Ro 16-8714 and protein in the diet with weight gain, carcass growth rate and food : gain ratio strongly indicate that optimum effects of β-AG on important growth parameters depend on protein supply. The improved killing out in pigs given low amounts of protein and receiving the β-AG can be explained by decreased weight of the non-carcass fraction and by enhanced muscle growth. Reduced weights of liver and of blood volume obtained at slaughter were likely the consequence of the combined effects of both β-AG and low protein intake.

The present study furthermore indicates

that stimulation of N retention by β-AG depends on protein supply. Thus, total N in the empty body was increased only in pigs receiving adequate amounts of protein. In addition, the reported shift of N from the non-carcass to the carcass fraction was enhanced at low protein intake if combined with β-AG administration.

It is unclear whether the reduced content of blood obtained at slaughter is the consequence of decreased production of blood cells or due to enhanced retention of blood in vessels. Reduced weight of internal organs could partly be the consequence of the drain of N (including amino acids) to the carcass fraction, but other factors may also contribute to this effect. Reduced spleen weight and possibly reduced leucocyte and lymphocyte formation could cause impaired immune responses. However, additional examinations with pigs of the present study revealed no evidence for altered immune response (lymphocyte stimulation *in vitro*, antibody response to horse erythrocytes) after 6 weeks of Ro 16-8714 administration in pigs given adequate or reduced amounts of protein (Hirni, Lazary and Blum, 1990). Additional studies are necessary to evaluate and consequence(s), if any, of the reduction of N retention (and perhaps of other nutrients) in the non-carcass fraction with respect to organ function.

The very high NPN : N ratio in the intestinal fraction of pigs was surprising and may be explained by protein breakdown in the period between recovering the tissues from the pigs and analysis. However, the NPN : N ratio of the intestine, as in other organs and in the carcass, was not affected by protein intake or by the β-AG. The reduced NPN : N ratio of blood of pigs given low amounts of protein and receiving the β-AG may have been in part an expression of a decrease of urea levels because β-AG can lower blood urea concentrations (Berschauer *et al.*, 1987; Bracher-Jakob *et al.*, 1990), an effect which was possibly enhanced during low protein feeding.

Only few data are presently available on interactions between β-AG and nutrition, i.e. feeding level (Kim, Lee and Dalrymple, 1987), restricted and *ad libitum* feeding (Bracher-Jakob *et al.*, 1990; Kim *et al.*, 1987, and Kim *et al.*, 1989), fat intake (Jones, Waitt, Mowrey and Anderson, 1988) and protein intake (Jones, Waitt, Mowrey and Anderson, 1987; Mersmann *et al.*, 1987; Anderson, Paxton and Mowrey, 1989; Inkster, Hovell, Kyle, Brown and Lobley, 1989). Inkster *et al.* (1989) suggested that β-AG (clenbuterol) could enhance the contribution of internal organs to N-flux in sheep given adequate amounts of energy (by intraruminal infusion of volatile fatty acids) but no N, an idea supported by our data obtained with pigs given reduced amounts of protein. In the study of Mersmann *et al.* 1987) young pigs (10 to 60 kg) were given insufficient or adequate amounts of protein (140 and 180 g/kg crude protein, respectively) and several measures of growth performance of the animals (daily gain, food intake, food : gain ratio, carcass length, protein and fat retention) were typically modified by protein intake. Surprisingly, the β-AG (cimaterol) did not significantly change daily weight gain, food : gain ratio, carcass length, protein and fat content and there was no evidence for protein sparing by the β-AG. Therefore, the data cannot directly be compared with those of our experiment with older pigs. In the study of Jones *et al.* (1987) with finishing pigs (65 to 105 kg BW), considerably higher amounts of crude protein (160, 200 or 240 g/kg, respectively) were offered compared with our experiment. Under these conditions of a surplus of protein — different from the conditions of our experiment — the β-AG (ractopamine) enhanced average daily gain, food : gain ratio, reduced fat retention and improved carcass leanness. Although protein intake did not significantly modify the effect of the β-AG, with increasing protein intake (from 160 to 200 or 240 g/kg crude protein) there was a numerical increase in average daily gain (by 100, 117 and 114 g/kg, respectively), dressing (by 11, 18 and 27 g/kg, respectively) and 10th rib loin-eye-area (by a factor of 1·23, 1·63 and 1·74, respectively), whereas leaf fat (by −215, −259 and −321 g/kg, respectively) and 10th rib fat (by −220, −221 and −246 g/kg, respectively) tended to decrease in the presence as compared with the absence of the β-AG.

Taken together, these and our data indicate that an adequate protein supply is needed for optimum effects of β-AG on growth performance and body composition and particularly on N retention. Further studies are necessary to define clearly protein and essential amino acids requirements in the presence of β-AG. Requirements may be elevated above norms, as shown when growth hormone is administered to growing pigs (Steele, Campbell, Caperna, McMurtry and Solomon, 1989; Boyd, Wray-Cahen and Krick, 1989).

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